

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

DATE:	20 Feb. 2006
FORMALITIES:	C.N. R.P.
PAT. OFF:	V.A
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FILE NO:	PU0404-PCT

To:

Amersham Biosciences AB
Patents Department
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RECEIVED

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WRITTEN OPINION OF THE
INTERNATIONAL PRELIMINARY
EXAMINING AUTHORITY

(PCT Rule 66)

Applicant's or agent's file reference PU0404 - PCT ~		Date of mailing (day/month/year) 22 -12- 2005
International application No. PCT/SE2005/000085 ~	International filing date (day/month/year) 26-01-2005 ~	Priority date (day/month/year) 29-01-2004
International Patent Classification (IPC) or both national classification and IPC See Supplemental Box		
Applicant Amersham Biosciences AB et al		

- ☒ The written opinion established by the International Searching Authority:
☒ is ☐ is not
considered to be a written opinion of the International Preliminary Examining Authority.
- This second (first, etc.) opinion contains indications relating to the following items:
 - ☒ Box No. I Basis of the opinion
 - ☐ Box No. II Priority
 - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - ☐ Box No. IV Lack of unity of invention
 - ☒ Box No. V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - ☐ Box No. VI Certain documents cited
 - ☐ Box No. VII Certain defects in the international application
 - ☒ Box No. VIII Certain observations on the international application
- The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(e).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4bis. For an informal communication with the examiner, see Rule 66.6. For an additional opportunity to submit amendments, see Rule 66.4.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
- The final date by which the international preliminary report on patentability (Chapter II of the PCT) must be established according to Rule 69.2 is: 29-05-2006

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**WRITTEN OPINION OF THE
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY**

International application No.

PCT/SE2005/000085

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: **Cover sheet**

INTERNATIONAL PATENT CLASSIFICATION (IPC) :

G01N 30/72 (2006.01)

B01D 15/08 (2006.01)

WRITTEN OPINION OF THE
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/SE2005/000085

Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____,
which is the language of a translation furnished for the purposes of:
☐ international search (Rules 12.3(a) and 23.1(b))
☐ publication of the international application (Rule 12.4(a))
☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this opinion has been established on the basis of (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."*):

- ☒ the international application as originally filed/furnished
☐ the description:
pages _____ as originally filed/furnished
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____
☐ the claims:
pages _____ as originally filed/furnished
pages _____ as amended (together with any statement) under Article 19
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____
☐ the drawings:
pages _____ as originally filed/furnished
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____
☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

4. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

WRITTEN OPINION OF THE
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.

PCT/SE2005/000085

Box No. V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	<u>18, 19 (NO)</u>
	Claims	
Inventive step (IS)	Claims	<u>18-23 (NO)</u>
	Claims	
Industrial applicability (IA)	Claims	
	Claims	

2. Citations and explanations:

The present application relates to a method for reducing the complexity of a biological sample and a system for performing said method. The complexity is reduced by selecting a fraction from the entire native or digested biological sample after a first separation (e.g. by anion exchange chromatography (AEC), isoelectric focussing or chromatofocussing), said fraction containing peptides which have a pI-value within a limited range and which fraction represents a subset of or the entire substance population in the sample. Said fraction is separated further by a second separation (e.g. cation exchange chromatography (CEC)). Thereafter, the separated components are analysed by mass spectrometry (MS).

The expression in claim 1(a), "a subset of", is considered to be contradictory to the inventive thought of the application, as stated in the definition of "total sample complexity reduction" on page 6 of the description. See also Box VIII.

Reference will be made to the following documents cited in the International Search Report:

- D1) US 5416023
- D2) Nature Biotechnology, 19:242-247 (2001), Washburn et al.
- D3) Electrophoresis, 23:3143-3148 (2002), Chen et al.
- D4) J Chromatog B, 787:11-18 (2003), Wang & Hanash

...//...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: BOX V

D1 discloses a system comprising a column combination comprising an anion exchange medium, a cation exchange medium and a reverse-phase medium (see claim 1).

The system according to claims 18-19 lacks novelty. It is defined by its components and does not obtain novelty merely due to its field of application.

The system according to claims 20-23 is novel.

D1 is considered to represent the closest prior art.

The system of claim 21 differs from what is disclosed in D1 in that the charge-selective column is a chromatofocussing column instead of an anion exchange column.

The system of claim 22 differs from what is disclosed in D1 in that the charge-selective column is an isoelectric focussing column instead of an anion exchange column.

However, said differences are not considered to represent solutions which involve an inventive step. It is obvious for the person skilled in the art to construct a system comprising a chromatofocussing column or an isoelectric focussing column instead of an anion exchange column. All components of the system are previously known in the art.

Consequently, the system according to claims 21-22 is considered to lack inventive step.

The system according to claims 20 and 23 differs from what is known from D1 in that the pH-values of the buffers used for the charge-selective column and the cation exchange column, respectively, are described.

However, said differences are not considered to represent solutions which involve an inventive step. The system according to claims 20 and 23 is not considered to be sufficiently adapted to the method of claims 1-17. It is doubted that the system contains all technical features which are needed in order to perform the method successfully. Therefore, the system of claims 20 and 23 is considered to lack inventive step.

...//...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: BOX V

D2 describes a large-scale analysis of the yeast proteome by multidimensional protein identification technology (see page 246, column 2, paragraphs 3-5).

D3 relates to the use of capillary isoelectric focusing and capillary reversed-phase liquid chromatography for two-dimensional proteomics separation (page 3144, column 2, paragraph 2; page 3145, column 1, paragraph 1; page 3147, column 1, paragraph 1).

D4 describes multi-dimensional liquid phase based separations in proteomics (see the entire document).

Documents D2, D3 and D4 represent prior art and are not considered to be relevant for the assessment of novelty and inventive step of the method according to claims 1-17 or the system according to claims 18-23.

The method of claims 1-17 is novel.

If the expression "a subset of" is removed from claim 1(a), the method of claims 1-17 will be considered to involve an inventive step.

**WRITTEN OPINION OF THE
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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The embodiment of claim 1(a) comprising "a subset of" the substance population is not considered to be fully supported by the description (Article 6 PCT). See also Box V.